



case serves to increase awareness and the need for antifungal stewardship, and highlights a potentially serious infectious disease and public health issue.

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## References

- 1 Clinical and Laboratory Standards Institute. Reference method for broth dilution antifungal susceptibility testing of filamentous fungi. Available at: <https://clsi.org/standards/products/microbiology/documents/m38/> (last accessed 31 July 2020).
- 2 Dogra S, Uprety S. The menace of chronic and recurrent dermatophytosis in India: is the problem deeper than we perceive? *Indian Dermatol Online J* 2016; **7**:73–6.
- 3 Mukherjee PK, Leidich SD, Isham N et al. Clinical *Trichophyton rubrum* strain exhibiting primary resistance to terbinafine. *Antimicrob Agents Chemother* 2003; **47**:82–6.
- 4 Digby SS, Hald M, Arendrup MC et al. Darier disease complicated by terbinafine-resistant *Trichophyton rubrum*: a case report. *Acta Derm Venereol* 2017; **97**:139–40.
- 5 Ghelardi E, Celandroni F, Gueye SA et al. Potential of ergosterol synthesis inhibitors to cause resistance or cross-resistance in *Trichophyton rubrum*. *Antimicrob Agents Chemother* 2014; **58**:2825–9.
- 6 Favre B, Ghannoum MA, Ryder NS. Biochemical characterization of terbinafine-resistant *Trichophyton rubrum* isolates. *Med Mycol* 2004; **42**:525–9.
- 7 Yamada T, Maeda M, Alshahni MM et al. Terbinafine resistance of *Trichophyton* clinical isolates caused by specific point mutations in the squalene epoxidase gene. *Antimicrob Agents Chemother* 2017; **61**: e00115–17.
- 8 Singh A, Masih A, Khurana A et al. High terbinafine resistance in *Trichophyton interdigitale* isolates in Delhi, India harbouring mutations in the squalene epoxidase gene. *Mycoses* 2018; **61**:477–84.

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## What is successful repigmentation in vitiligo from the point of view of patients?

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DEAR EDITOR, Based on an international e-Delphi consensus, repigmentation has been defined as a core outcome in vitiligo.<sup>1</sup>

Many measurement instruments have been used to assess repigmentation;<sup>2</sup> to date, the Vitiligo Extent Score and the Vitiligo Area Severity Index are the best validated.<sup>3,4</sup>

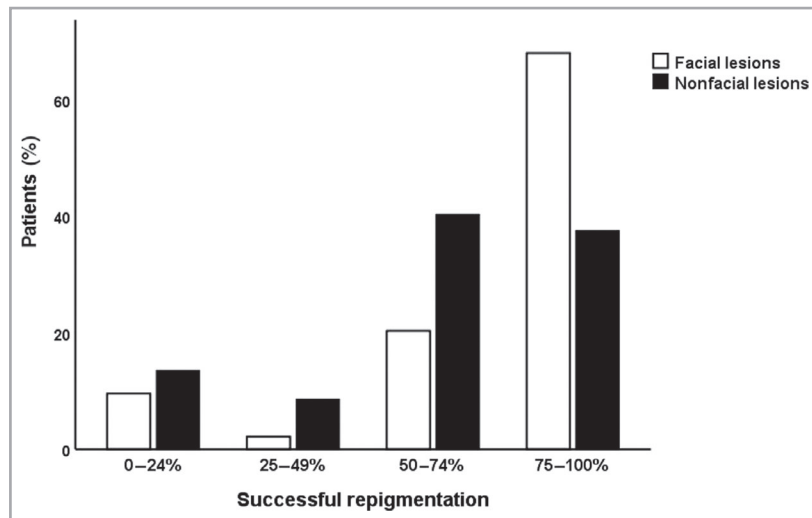
However, for interpretation of this outcome, little evidence is available on the thresholds of successful repigmentation. In previous Cochrane reviews on vitiligo, success was arbitrarily defined as > 75% repigmentation.<sup>5</sup> But why was 75% chosen as the limit? In atopic eczema and psoriasis, the Psoriasis Area and Severity Index 75% and the Eczema Area and Severity Index 75% are commonly used to define successful treatment.<sup>6,7</sup> However, in vitiligo – where treatments generally yield less improvement – this analogy may not be true. Previous clinical studies defined successful repigmentation varying from ‘any repigmentation’ to a 100% repigmentation, and was usually defined by physicians.<sup>2</sup> Until now, little has been known on patients’ perspectives regarding successful treatment in terms of repigmentation. In addition, these success percentages could differ depending on location. Remarkably, Eleftheriadou et al. showed, in three focus groups, that unanimous agreement was reached in all participants with vitiligo that 80–100% repigmentation of a target lesion was regarded as successful.<sup>8</sup>

We aimed to evaluate the definition of successful repigmentation for facial and nonfacial lesions from the patient’s perspective by carrying out a prospective cross-sectional questionnaire study.

All patients aged ≥ 16 years with nonsegmental vitiligo who had consecutively visited our outpatient clinic at the Netherlands Institute for Pigment Disorders of the Amsterdam University Medical Center between April 2017 and January 2019 were asked to complete a secure online questionnaire (LimeSurvey version 2.6.7). Written informed consent was obtained from all patients. This survey consisted of questions regarding patient demographics, quality of life and successful repigmentation rates concerning the patient’s own situation. Answers were based on a visual analogue scale ranging from 0% to 100%, with separate questions for facial and nonfacial lesions (on the body). Only fully completed questionnaires were included in the analysis. This study was not subject to the Medical Research Involving Human Subjects Act, as confirmed by the Ethics Committee of the Amsterdam UMC (W17\_349).

The overall response rate was 70% (n = 377; 60% fully completed, 8% not completed, 2% declined). The male:female ratio was 135 : 192, median age was 40 years (range 16–77) and median disease duration was 7 years. Facial lesions were present in 86% of participants and nonfacial lesions in 70%. Eighty-three per cent of patients had a light skin type (Fitzpatrick I–III) and 17% had a dark skin type (Fitzpatrick IV–VI). Median Dermatology Life Quality Index total score was 2 (interquartile range 1–6).

Of the 325 patients that completed the questionnaire, 221 (68%) and 122 (37%) patients considered ≥ 75% repigmentation successful for their facial vitiligo and nonfacial vitiligo lesion(s), respectively (Figure 1). The success threshold for facial lesions in patients with a dark skin type was significantly



**Figure 1** Percentage repigmentation regarded as successful by patients for facial and nonfacial lesions. The bar graph represents the percentages in repigmentation that patients with vitiligo have reported to be regarded as successful for facial lesions (white bars) and for lesions on the body (black bars). The y-axis represents the percentage of the total number of patients.

higher compared with patients with a light skin type (median 90% vs. 80%;  $P_{\text{Mann-Whitney U-test}} = 0.018$ ). The same applied to nonfacial lesions (dark skin type 70% vs. light skin type 50%,  $P_{\text{Mann-Whitney U-test}} = 0.035$ ). Twenty-two per cent of patients reported that 100% repigmentation should be regarded as successful for facial vitiligo.

Our results are largely in agreement with the study of Eleftheriadou *et al.*<sup>8</sup> Remarkably, one in five patients only regards treatment successful if 100% of the facial lesions are repigmented. However, a considerable proportion also seem to be content with lower repigmentation rates, indicating a great variation in our population. In addition, for nonfacial lesions, patients seem to be less critical and were satisfied with less repigmentation.

There are some limitations to this study. This questionnaire was constructed specifically for this study and was not validated. Moreover, as patients were included at a national referral centre, the patient population in this study may not fully reflect the larger community of people with vitiligo who do not seek care or are not referred to our centre. However, the strengths of this study include the large cross-sectional group of patients and the specification of facial vs. nonfacial lesions. In addition, patients were able to complete the questionnaire at home without potential influences.

This study indicates that there is a great variety among patients regarding their definitions of successful repigmentation. Furthermore, successful repigmentation seems to depend on the location of the lesions and on skin type. In line with a previous focus group study, we found that only a high percentage of repigmentation ( $\geq 75\%$ ) in the face is regarded as successful by the majority of the patients. For future research we recommend involving different ethnicities and more patients with a dark skin type, to determine successful repigmentation.

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## References

- 1 Eleftheriadou V, Thomas K, van Geel N *et al.* Developing core outcome set for vitiligo clinical trials: international e-Delphi consensus. *Pigment Cell Melanoma Res* 2015; **28**:363–9.
- 2 Eleftheriadou V, Thomas KS, Whitton ME *et al.* Which outcomes should we measure in vitiligo? Results of a systematic review and a survey among patients and clinicians on outcomes in vitiligo trials. *Br J Dermatol* 2012; **167**:804–14.
- 3 van Geel N, Lommerts J, Bekkenk M *et al.* Development and validation of the Vitiligo Extent Score (VES): an international collaborative initiative. *J Invest Dermatol* 2016; **136**:978–84.
- 4 Komen L, van der Kraaij GE, van der Veen JPW *et al.* The validity, reliability and acceptability of the SAVASI; a new self-assessment score in vitiligo. *J Eur Acad Dermatol Venereol* 2015; **29**:2145–51.
- 5 Whitton ME, Pinart M, Batchelor J *et al.* Interventions for vitiligo. *Cochrane Database Syst Rev* 2015; **2**:CD003263.
- 6 Carlin CS, Feldman SR, Krueger JG *et al.* A 50% reduction in the Psoriasis Area and Severity Index (PASI 50) is a clinically significant endpoint in the assessment of psoriasis. *J Am Acad Dermatol* 2004; **50**:859–66.
- 7 Snast I, Reiter O, Hodak E *et al.* Are biologics efficacious in atopic dermatitis? A systematic review and meta-analysis. *Am J Clin Dermatol* 2018; **19**:145–65.
- 8 Eleftheriadou V, Hamzavi I, Pandya AG *et al.* International Initiative for Outcomes (INFO) for vitiligo: workshops with patients with vitiligo on repigmentation. *Br J Dermatol* 2019; **180**:574–9.

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